



essential thrombocythemia

Essential thrombocythemia is a condition characterized by an increased number of platelets (thrombocythemia). Platelets (thrombocytes) are blood cell fragments involved in blood clotting. While some people with this condition have no symptoms, others develop problems associated with the excess platelets.

Abnormal blood clotting (thrombosis) is common in people with essential thrombocythemia and causes many signs and symptoms of this condition. Clots that block blood flow to the brain can cause strokes or temporary stroke-like episodes known as transient ischemic attacks. Thrombosis in the legs can cause leg pain, swelling, or both. In addition, clots can travel to the lungs (pulmonary embolism), blocking blood flow in the lungs and causing chest pain and difficulty breathing (dyspnea).

Another problem in essential thrombocythemia is abnormal bleeding, which occurs more often in people with a very high number of platelets. Affected people may have nosebleeds, bleeding gums, or bleeding in the gastrointestinal tract. It is thought that bleeding occurs because a specific protein in the blood that helps with clotting is reduced, although why the protein is reduced is unclear.

Other signs and symptoms of essential thrombocythemia include an enlarged spleen (splenomegaly); weakness; headaches; or a sensation in the skin of burning, tingling, or prickling. Some people with essential thrombocythemia have episodes of severe pain, redness, and swelling (erythromelalgia), which commonly occur in the hands and feet.

Frequency

Essential thrombocythemia affects an estimated 1 to 24 per 1 million people worldwide.

Genetic Changes

The *JAK2* and *CALR* genes are the most commonly mutated genes in essential thrombocythemia. The *MPL*, *THPO*, and *TET2* genes can also be altered in this condition. The *JAK2*, *MPL*, and *THPO* genes provide instructions for making proteins that promote the growth and division (proliferation) of blood cells. The *CALR* gene provides instructions for making a protein with multiple functions, including ensuring the proper folding of newly formed proteins and maintaining the correct levels of stored calcium in cells. The *TET2* gene provides instructions for making a protein whose function is unknown.

The proteins produced from the *JAK2*, *MPL*, and *THPO* genes are part of a signaling pathway called the JAK/STAT pathway, which transmits chemical signals from outside

the cell to the cell's nucleus. These proteins work together to turn on (activate) the JAK/STAT pathway, which promotes the proliferation of blood cells, particularly platelets and their precursor cells, megakaryocytes.

Mutations in the *JAK2*, *MPL*, and *THPO* genes that are associated with essential thrombocythemia lead to overactivation of the JAK/STAT pathway. The abnormal activation of JAK/STAT signaling leads to overproduction of megakaryocytes, which results in an increased number of platelets. Excess platelets can cause thrombosis, which leads to many signs and symptoms of essential thrombocythemia.

Although mutations in the *CALR* and *TET2* genes have been found in people with essential thrombocythemia, it is unclear how these gene mutations are involved in development of the condition.

Some people with essential thrombocythemia do not have a mutation in any of the known genes associated with this condition. Researchers are working to identify other genes that may be involved in the condition.

Inheritance Pattern

Most cases of essential thrombocythemia are not inherited. Instead, the condition arises from gene mutations that occur in early blood-forming cells after conception. These alterations are called somatic mutations.

Less commonly, essential thrombocythemia is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. When it is inherited, the condition is called familial essential thrombocythemia.

Other Names for This Condition

- essential thrombocytosis
- primary thrombocythemia
- primary thrombocytosis

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Essential thrombocythemia
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0040028/>

Other Diagnosis and Management Resources

- Cleveland Clinic: Thrombocytosis
<http://my.clevelandclinic.org/health/articles/thrombocytosis>
- Merck Manual for Health Care Professionals: Essential Thrombocythemia
<http://www.merckmanuals.com/professional/hematology-and-oncology/myeloproliferative-disorders/essential-thrombocythemia>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Primary Thrombocythemia
<https://medlineplus.gov/ency/article/000543.htm>
- Encyclopedia: Splenomegaly
<https://medlineplus.gov/ency/article/003276.htm>
- Health Topic: Bone Marrow Diseases
<https://medlineplus.gov/bonemarrowdiseases.html>
- Health Topic: Platelet Disorders
<https://medlineplus.gov/plateletdisorders.html>

Genetic and Rare Diseases Information Center

- Essential thrombocythemia
<https://rarediseases.info.nih.gov/diseases/6594/essential-thrombocythemia>

Additional NIH Resources

- National Cancer Institute: Essential Thrombocythemia
https://www.cancer.gov/types/myeloproliferative/patient/chronic-treatment-pdq#section/_245
- National Heart Lung and Blood Institute: What are Thrombocythemia and Thrombocytosis?
<https://www.nhlbi.nih.gov/health/health-topics/topics/thrm/>

Educational Resources

- Cleveland Clinic: Thrombocytosis
<http://my.clevelandclinic.org/health/articles/thrombocytosis>
- Disease InfoSearch: Essential Thrombocythemia
<http://www.diseaseinfosearch.org/Essential+Thrombocythemia/2660>
- Leukemia and Lymphoma Society: Essential Thrombocythemia
<http://www.lls.org/myeloproliferative-neoplasms/essential-thrombocythemia>
- Leukemia and Lymphoma Society: Normal Blood and Marrow
<http://www.lls.org/managing-your-cancer/understanding-blood-marrow-and-the-lymphatic-system/normal-blood-and-marrow>
- MalaCards: essential thrombocythemia
http://www.malacards.org/card/essential_thrombocythemia
- Merck Manual for Health Care Professionals: Essential Thrombocythemia
<http://www.merckmanuals.com/professional/hematology-and-oncology/myeloproliferative-disorders/essential-thrombocythemia>
- Myeloproliferative Neoplasm (MPN) Research Foundation: Essential Thrombocythemia
<http://www.mpnresearchfoundation.org/Essential-Thrombocythemia>

Patient Support and Advocacy Resources

- Leukemia and Lymphoma Society
<http://www.lls.org/>
- Myeloproliferative Neoplasm (MPN) Education Foundation
<http://mpninfo.org/index.php>
- Myeloproliferative Neoplasm (MPN) Research Foundation
<http://www.mpnresearchfoundation.org/>
- National Organization for Rare Disorders (NORD): Essential Thrombocythemia
<https://rarediseases.org/rare-diseases/essential-thrombocythemia/>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22essential+thrombocythemia%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Thrombocythemia,+Essential%5BMAJR%5D%29+AND+%28essential+thrombocythemia%5BTI%5D%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

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<http://omim.org/entry/187950>

Sources for This Summary

- Chaligné R, Tonetti C, Besancenot R, Roy L, Marty C, Mossuz P, Kiladjian JJ, Socié G, Bordessoule D, Le Bousse-Kerdilès MC, Vainchenker W, Giraudier S. New mutations of MPL in primitive myelofibrosis: only the MPL W515 mutations promote a G1/S-phase transition. *Leukemia*. 2008 Aug;22(8):1557-66. doi: 10.1038/leu.2008.137. Epub 2008 Jun 5.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18528423>
- Ding J, Komatsu H, Iida S, Yano H, Kusumoto S, Inagaki A, Mori F, Ri M, Ito A, Wakita A, Ishida T, Nitta M, Ueda R. The Asn505 mutation of the c-MPL gene, which causes familial essential thrombocythemia, induces autonomous homodimerization of the c-Mpl protein due to strong amino acid polarity. *Blood*. 2009 Oct 8;114(15):3325-8. doi: 10.1182/blood-2008-04-149047. Epub 2009 May 29.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19483125>
- Klampfl T, Gisslinger H, Harutyunyan AS, Nivarthi H, Rumi E, Milosevic JD, Them NC, Berg T, Gisslinger B, Pietra D, Chen D, Vladimer GI, Bagienski K, Milanese C, Casetti IC, Sant'Antonio E, Ferretti V, Elena C, Schischlik F, Cleary C, Six M, Schalling M, Schönegger A, Bock C, Malcovati L, Pascutto C, Superti-Furga G, Cazzola M, Kralovics R. Somatic mutations of calreticulin in myeloproliferative neoplasms. *N Engl J Med*. 2013 Dec 19;369(25):2379-90. doi: 10.1056/NEJMoa1311347. Epub 2013 Dec 10.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24325356>
- Majka M, Ratajczak J, Villaire G, Kubiczek K, Marquez LA, Janowska-Wieczorek A, Ratajczak MZ. Thrombopoietin, but not cytokines binding to gp130 protein-coupled receptors, activates MAPKp42/44, AKT, and STAT proteins in normal human CD34+ cells, megakaryocytes, and platelets. *Exp Hematol*. 2002 Jul;30(7):751-60.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12135673>
- Merck Manual for Health Care Professionals: Essential Thrombocythemia
<http://www.merckmanuals.com/professional/hematology-and-oncology/myeloproliferative-disorders/essential-thrombocythemia>

- Nangalia J, Massie CE, Baxter EJ, Nice FL, Gundem G, Wedge DC, Avezov E, Li J, Kollmann K, Kent DG, Aziz A, Godfrey AL, Hinton J, Martincorena I, Van Loo P, Jones AV, Guglielmelli P, Tarpey P, Harding HP, Fitzpatrick JD, Goudie CT, Ortmann CA, Loughran SJ, Raine K, Jones DR, Butler AP, Teague JW, O'Meara S, McLaren S, Bianchi M, Silber Y, Dimitropoulou D, Bloxham D, Mudie L, Maddison M, Robinson B, Keohane C, Maclean C, Hill K, Orchard K, Tauro S, Du MQ, Greaves M, Bowen D, Huntly BJ, Harrison CN, Cross NC, Ron D, Vannucchi AM, Papaemmanuil E, Campbell PJ, Green AR. Somatic CALR mutations in myeloproliferative neoplasms with nonmutated JAK2. *N Engl J Med*. 2013 Dec 19;369(25):2391-405. doi: 10.1056/NEJMoa1312542. Epub 2013 Dec 10.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24325359>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3966280/>
- Rumi E, Pietra D, Ferretti V, Klampfl T, Harutyunyan AS, Milosevic JD, Them NC, Berg T, Elena C, Casetti IC, Milanese C, Sant'antonio E, Bellini M, Fugazza E, Renna MC, Boveri E, Astori C, Pascutto C, Kralovics R, Cazzola M; Associazione Italiana per la Ricerca sul Cancro Gruppo Italiano Malattie Mieloproliferative Investigators. JAK2 or CALR mutation status defines subtypes of essential thrombocythemia with substantially different clinical course and outcomes. *Blood*. 2014 Mar 6;123(10):1544-51. doi: 10.1182/blood-2013-11-539098. Epub 2013 Dec 23.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24366362>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3945864/>
- Saint-Martin C, Leroy G, Delhommeau F, Panelatti G, Dupont S, James C, Plo I, Bordessoule D, Chomienne C, Delannoy A, Devidas A, Gardembas-Pain M, Isnard F, Plumelle Y, Bernard O, Vainchenker W, Najman A, Bellanné-Chantelot C; French Group of Familial Myeloproliferative Disorders. Analysis of the ten-eleven translocation 2 (TET2) gene in familial myeloproliferative neoplasms. *Blood*. 2009 Aug 20;114(8):1628-32. doi: 10.1182/blood-2009-01-197525. Epub 2009 Jun 29.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19564637>
- Tefferi A, Pardanani A, Lim KH, Abdel-Wahab O, Lasho TL, Patel J, Gangat N, Finke CM, Schwager S, Mullally A, Li CY, Hanson CA, Mesa R, Bernard O, Delhommeau F, Vainchenker W, Gilliland DG, Levine RL. TET2 mutations and their clinical correlates in polycythemia vera, essential thrombocythemia and myelofibrosis. *Leukemia*. 2009 May;23(5):905-11. doi: 10.1038/leu.2009.47. Epub 2009 Mar 5.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19262601>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4654629/>
- Tefferi A. Novel mutations and their functional and clinical relevance in myeloproliferative neoplasms: JAK2, MPL, TET2, ASXL1, CBL, IDH and IKZF1. *Leukemia*. 2010 Jun;24(6):1128-38. doi: 10.1038/leu.2010.69. Epub 2010 Apr 29. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20428194>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3035972/>
- Wiestner A, Schlemper RJ, van der Maas AP, Skoda RC. An activating splice donor mutation in the thrombopoietin gene causes hereditary thrombocythaemia. *Nat Genet*. 1998 Jan;18(1):49-52.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/9425899>

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